Life Cycle of HIV Infection

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HIV begins its infection of a susceptible host cell by binding to the CD4 receptor on the host cell. CD4 is present on the surface of many lymphocytes, which are a critical part of the body's immune system. Recent evidence indicates that a coreceptor is needed for HIV to enter the cell. This recognition of HIV coreceptors and progress in understanding how HIV fuses with the cell has opened up new possibilities for antiviral drugs. A number of new agents are being designed to prevent infection by blocking fusion of HIV with its host cell.

Following fusion of the virus with the host cell, HIV enters the cell. The genetic material of the virus, which is RNA, is released and undergoes reverse transcription into DNA. An enzyme in HIV called reverse transcriptase is necessary to catalyze this conversion of viral RNA into DNA. Inhibitors of reverse transcriptase, such as AZT, were the first anti-HIV medications, and are still a critical part of treating patients who have HIV. Reverse transcriptase inhibitors are divided into two classes-nucleoside analogues and non-nucleoside reverse transcriptase inhibitors-based on their structure and how they inhibit reverse transcriptase.

Once the genetic material of HIV has been changed into DNA, this viral DNA enters the host cell nucleus where it can be integrated into the genetic material of the cell. The enzyme integrase catalyzes this process, and inhibitors of integrase are under study as a new way to block HIV replication. Once the viral DNA is integrated into the genetic material of the host, it is possible that HIV may persist in a latent state for many years. This ability of HIV to persist in certain latently infected cells is the major barrier to eradication or cure of HIV. For this reason, based on our current knowledge, patients must remain on anti-viral therapy for life.

Activation of the host cells results in the transcription of viral DNA into messenger RNA (mRNA), which is then translated into viral proteins. The new viral RNA forms the genetic material of the next generation of viruses. The viral RNA and viral proteins assemble at the cell membrane into a new virus. Amongst the viral proteins is HIV protease, which is required to process other HIV proteins into their functional forms. Protease inhibitors, one of the most potent types of anti-viral medications, act by blocking this critical maturation step. Following assembly at the cell surface, the virus then buds forth from the cell and is released to infect another cell.

Unless the HIV lifecycle is interrupted by treatment, the virus infection spreads throughout the body and results in the destruction of the body's immune system. With current anti-viral medications, such as reverse transcriptase inhibitors and protease inhibitors, HIV infection can be contained. However, a great deal more must be achieved before AIDS epidemic is brought under control. One important immediate goal is to design new, more potent medications that are easier to take and have fewer side effects.

However, the ultimate challenges are to use our understanding of the HIV lifecycle to develop medications that will eradicate HIV from people who are already infected and to create a vaccine that will prevent new infections in the future.

Antiretroviral Agents Currently Available (generic name/Trade name)

Nucleoside Analogs

zidovudine/*Retrovir* (AZT, ZDV)

didanosine/*Videx, Videx EC* (ddI)

zalcitabine/*HIVID* (ddC)

stavudine/*Zerit* (d4T)

lamivudine/*Epivir* (3TC)

abacavir/*Ziagen* (ABC)

Non-Nucleoside Reverse Transcriptase Inhibitors

nevirapine/*Viramune* (NVP)

delavirdine/*Rescriptor* (DLV)

efavirenz/*Sustiva* (EFV)

Nucleotide Analogue

tenofovir DF/*Viread* (TDF)

Protease Inhibitors

indinavir/*Crixivan*

ritonavir/*Norvir*

saquinavir/*Invirase*, *Fortovase*

nelfinavir/*Viracept*

amprenavir/*Agenerase*

lopinavir/ritonavir, *Kaletra*
